REMARKS

Reconsideration and allowance are respectfully requested.

Claims 30-32 are pending.

35 U.S.C. 112 – Definiteness

Claims 30-32 were rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Action stated on page 2 that "it is not clear what present in the milligram amounts means, as a composition comprises a concentration of a particular item, such as grams/liter, for example" (Paper No. 12). Applicants traverse.

"If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more." Miles Laboratories, Inc. v. Shandon Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993), *citing* Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1375, 231 USPQ 81, 87 (Fed. Cir. 1986), *cert. denied,* 480 U.S. 947, 94 L.Ed.2d 792, 107 S.Ct. 1606 (1987). The rejected claims are directed to a pharmaceutical composition in which from 0.1 mg to 6 g of the recited globin chain is present in the composition, regardless of its concentration in the composition. There is no ambiguity as to whether a given composition is included or excluded from the claim and no reason has been given as to why the person of skill in the art would not understand the scope of the claim.

If the Examiner is basing this rejection on an allegation that the mass amount of a chemical (e.g., alpha and/or beta globin chain of hemoglobin) is not a permissible limitation in a claim directed to a composition, support for this assertion is requested. No legal authority or reasoning has been given for such assertion. Instead, page 2 of the Action stated, "It is standard chemical and pharmaceutical practice to recite concentrations when discussing compositions." But any such composition would also have a volume and one of ordinary skill in the art would be able to multiply concentration by volume to arrive at the mass of the chemical contained in the composition. Thus, it is equivalent to describe the amount of chemical in a composition by its concentration or

mass because such quantities can be converted from one to the other. Here, Applicants have described their invention by the mass of globin chain in the composition (see page 14, line 7, of the specification).

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 102 – Novelty

To be anticipated under Section 102, each and every element of a claim must be disclosed, either explicitly or inherently, in a single reference. Lewmar Marine, Inc., v. Barient, Inc., 827 F.2d 744, 747, 3 USPQ2d 1766, 1767 (Fed. Cir. 1987). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) *quoting* In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981). The extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999) *quoting* Continental Can *id.* at 1268, 20 USPQ2d at 1749.

Claims 30-32 were rejected under Section 102(b) as allegedly anticipated by Tame et al. (J. Mol. Biol. 218:761-767, 1991). Applicants traverse.

Page 3 of the Action (Paper No. 12) states, "Claims 30 to 32 are anticipated because there is no concentration provided in the claims, and enough of the solutions taught in Tame et al. can be made to comprise 0.1 mg to 6 g of globin." But this is insufficient basis to make a Section 102 rejection because the issue in anticipation is not what can be made, but what was made or disclosed. Tame et al. do not disclose the making of a solution containing from 0.1 mg to 6 g of alpha globin and/or beta globin. Here, the volume of the solution made by Tame et al. is not disclosed; only the concentration of the solution (5 mg/ml or 0.25 mg/ml) is taught. Therefore, lacking a disclosure of the solution's volume, Tame et al. do not disclose the range of masses recited in claims 30-32 and the cited reference does not anticipate the claimed invention. An anti-

cipation rejection cannot be based on probabilities or possibilities because the allegedly inherent limitation must be disclosed in the prior art reference. Robertson.

Claims 30-32 were rejected under Section 102(e) as allegedly anticipated by Hoffman et al. (U.S. Patent 5,449,759). Applicants traverse.

As in Tame et al. which was cited above, it is undisputed that Hoffman et al. do not disclose a composition containing the recited amount of any globin chain. Instead, the rejection is impermissibly based on what could be made. Thus, page 5 of the Action (Paper No. 12) states, "Just the single millimeter of Hoffman et al.'s solution meets the claim amount recitation." But Hoffman et al. do not teach or suggest a solution which is only one millimeter in volume. Instead, it was asserted in the Office Action that solutions containing alpha or beta globin at the concentrations disclosed by Hoffman et al. may be made at whatever volume is needed to anticipate the claims. This an imper-missible basis for a Section 102 rejection as noted above (see Robertson). Therefore, Hoffman et al. do not disclose each and every element of claims 30-32.

The incorrectness of the Office Action's argument that the solution can be made in sufficient quantity (i.e., volume) to anticipate the range of masses recited in the claims is shown from using the analogous argument to impermissibly extend the prior art with respect to the range of concentrations taught. Just as one could make whatever volume of solution is needed to arrive at a desired mass, one could dilute or enrich the solution sufficiently to achieve any desired concentration. A one milliliter solution of 1 mg/ml would allegedly "teach" not only a composition containing 1 mg, but any mass and any concentration as desired by the Patent Office. The reasoning used in the Office Action is clearly incorrect. Tame et al. and Hoffman et al. must have made their solutions in a particular volume(s). They are silent, however, on the volumes made so the solutions do not necessarily and inherently teach the claimed compositions.

A prior art reference does not anticipate a claim without actually or inherently teaching all of the claim limitations. Lewmar Marine. Here, the solutions of Tame et al. and Hoffmann et al. must have a volume and contain a certain mass of alpha or beta globin. But no evidence has been presented in the Office Action to show that the mass of alpha or beta globin in the solutions of the cited references would necessarily satisfy

the requirements of the claims and, thus, shift the burden to Applicants to prove otherwise. The mass of alpha or beta chain in their solutions is an inherent property of the solution, but it is not a quantity which can be manipulated at will by the Patent Office to produce the limitations of the claims.

It was twice stated on pages 4 and 5 of the Action, "This jug/beaker/vial/syringe of solution must have the alpha globin chain present in 0.1 mg to 6 g" (emphasis added) in reference to the disclosures of Tame et al. and Hoffman et al. As noted above, there was no indication in the cited references of the volumes of their solutions so allegations that a "single milliliter of [the cited reference's] solution[s] meets the claim amount recitation" (pages 4 and 5 of the Action) are mere speculations by the Patent Office and not supported by the evidence. It was further stated on pages 4 and 5 of the Action, "The composition must be suitable for subcutaneous administration, meaning it can be administered s.c." (emphasis added). But the human alpha globin chain was produced in *E. coli* in both cited references and purification of the apoproteins prior to inclusion of heme did not remove endotoxin which one of ordinary skill in the art would expect to be in the solutions of the cited references. Without such removal of a substance known to be dangerous to humans, it is clear that the solutions of the cited references are not suitable for subcutaneous administration. The unsubstantiated allegations of the Patent Office do not make up for this lack of evidence.

Best and Gray cited on page 5 of the Action are not relevant to this situation. In Gray, it was held that since the issue was "whether the prior art [human nerve growth] factor is identical or patentably distinct from that of the material on appeal, appellants have the burden of showing that inherency is not involved." Ex parte Gray, 10 USPQ2d 1922, 1925. But the issue here is not whether the globin chains required by the claims are identical to the alpha or beta globin of the cited references. Here, the protein components of the claimed compositions are identical to the isolated, native globin chains without heme. Moreover, Applicants have not discovered an inherent biological activity or function for the composition which was not described in the cited references. Cf. In re Best, 195 USPQ 430, 432-3. Instead, the mass of alpha and/or beta globin chains is a physical quantity and a limitation explicitly recited in claims 30-32, unlike the functional

limitations considered in Best and other cases dealing with inherency. The Patent Office has not provided sufficient grounds to shift the burden to Applicants because there was no evidence presented in the Office Action to indicate that the solutions described in the cited references were necessarily made in volumes which would result in the "identical or substantially identical" mass of alpha and/or beta globin chain recited in the pending claims. If this rejection is maintained, the Examiner is requested to cite the evidence which supports her allegation that the solutions of Tame et al. and Hoffman et al. were made in amounts within the range recited in the claims.

The Manual of Patent Examining Procedure discusses the circumstances under which the prior art may anticipate a composition claim which recites a range such as 0.1 mg to 6 g. M.P.E.P. § 2131.03 ("In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with 'sufficient specificity to constitute an anticipation under the statute.'"). Here, Tame et al. and Hoffman et al. are silent on the mass of globin chain in their compositions. The references' disclosure of a concentration and the assertion by the Patent Office that "enough of the solutions . . . can be made" does not provide sufficient specificity to anticipate the range of masses which is recited in the pending claims.

In the absence of reasoning or extrinsic evidence that the prior art disclosed compositions with alpha and/or beta globin chain in an amount of 0.1 mg to 6 g as an inherent characteristic, the burden does not shift to Applicants to prove otherwise.

Withdrawal of the Section 102 rejections is requested because all limitations of the claimed invention are not disclosed by the cited reference.

Conclusion

Having fully responded to all of the pending objections and rejections contained in the Office Action (Paper No. 12), Applicants submit that the claims are in condition for

allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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